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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/524,462

10/18/2005

Gordon Weingarten

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05/25/2006

EXAMINER

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ART UNIT

PAPER NUMBER

1624

DATE MAILED: 05/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/524,462

Applicant(s)

WEINGARTEN ET AL.

Examiner

Venkataraman Balasubramanian

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 March 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9,11-14,20 and 23-40 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-9,11,14,20,27-31 and 36-40 is/are allowed.
- 6) ☒ Claim(s) 12,13,23-26 and 32-35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 3/13/2006.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

DETAILED ACTION

Applicants' response, which included cancellation of claims 10,15-19, 21 and 22, addition of new claims 23-40 and amendment to claims 1, 2, 12 and 13, filed on 3/13/2006, is made of record. Claims 1-9, 11-4, 20 and 23-40 are now pending.

In view of applicants' response, all 112 second and first paragraph rejections have been obviated and or rendered moot. However, the following new grounds of rejection apply.

Information Disclosure Statement

References cited in the Information Disclosure Statement , filed on 3/13/2006, are made of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12 and 13 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Recitation of "interconverting the compound of formula (I) into another compound of formula (I) and deprotecting derivative of compound of formula (I) in claim 12 and 13 renders these claims vague and unclear as to what is intended. If step A to produce compound of formula (I) what is not included in this compound of formula (I) that is being transformed in subsequent step B. Similarly, step A is not including a derivative of the compound of formula I and hence the need for step C is unclear.

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23-26 and 32-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating pain due to headache or arthritis, does not reasonably provide enablement for treating any or all acute or chronic pain originating from various diseases generically embraced in the claim language. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Following reasons apply.

As recited, claims 23-26 and 32-35 are reach through claims. Reach through claims, in general have a format drawn to mechanistic, receptor binding or enzymatic functionality and thereby reach through any or all diseases, disorders or conditions for which they lack written description and enabling disclosure in the specification. In the instant case, because of the inhibition of COX-2 activity shown by compound formula I, it is recited that instant compounds are useful for treatment of any or all pain caused by any or all diseases including neurodegenerative diseases and cancers, for which there is no adequate written description and enabling disclosure in the instant specification.

The scope of the claims includes treating any or all pain arising from various diseases and disorders as mediated by COX-2 for which there is no enabling disclosure. In addition, the scope of these claims includes treating acute and chronic pain of any origin and would include lower back and neck pain, headache, toothache,

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sympathetically maintained pain, neuropathic pain syndromes include: diabetic neuropathy; sciatica, non-specific lower back pain; multiple sclerosis pain, fibromyalgia, HIV-related neuropathy neuralgia, such as post-herpetic neuralgia and trigeminal neuralgia; and pain resulting from physical trauma, amputation, cancer, toxins or chronic inflammatory conditions. These conditions are difficult to treat and although several drugs are known to have limited efficacy, complete pain control is rarely achieved. The symptoms of neuropathic pain are incredibly heterogeneous and are often described as spontaneous shooting and lancinating pain, or ongoing, burning pain. In addition, there is pain associated with normally non-painful sensations such as "pins and needles" (paraesthesias and dysesthesias), increased sensitivity to touch (hyperesthesia), painful sensation following innocuous stimulation (dynamic, static or thermal allodynia), increased sensitivity to noxious stimuli (thermal, cold, mechanical hyperalgesia), continuing pain sensation after removal of the stimulation (hyperpathia) or an absence of or deficit in selective sensory pathways (hypoalgesia), etc., which are not adequately enabled solely based on the inhibiting COX-2 activity of the compounds provided in the specification at pages 1-8 and 24. The instant compounds are disclosed to have inhibiting COX-2 activity and it is recited that the instant compounds are therefore useful in treating any or all acute and chronic pain where COX-2 activity is implicated, for which applicants provide no competent evidence. Furthermore, the applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by the claim language for the intended host. The scope of the claims involves all of the thousands of compounds

of instant claims as well as the thousand of diseases causing pain both acute and chronic embraced by the terms inflammatory diseases, non-vascular syndromes etc

Inflammation is a process that can take place in virtually any part of the body. There is a vast range of forms that it can take, causes for the problem, and biochemical pathways that mediate the inflammatory reaction. There is no common mechanism by which all, or even most, inflammations arise. Mediators include bradykinin, serotonin, C3a, C5a, histamine, leukotrienes, cytokines, and many, many others. Accordingly, treatments for inflammation are normally tailored to the particular type of inflammation present, as there is no, and there can be no "magic bullet" against inflammation generally. There is a vast range of forms that it can take,' causes for the problem, and biochemical pathways that mediate the inflammatory reaction. There are hundreds such diseases, which have fundamentally different mechanisms and different underlying causes. Thus, the scope of claims is extremely broad.

No compound has ever been found to treat all types of pain. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits.

Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See *Ex parte Jovanovics*, 211 USPQ 907, 909; *In re Langer* 183 USPQ 288. Also note *Hoffman v. Klaus* 9 USPQ 2d 1657 and *Ex parte Powers* 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 64 FR 71427 and 71440 (December 21, 1999) wherein it is

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emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method treating solely based on the inhibitory activity disclosed for the compounds.

The state of the art at the time of instant invention is indicative of the requirement for undue experimentation. See *Stichtenoth et al.*, *Drugs*, 63(1): 33-45, 2003 and *Hochberg MC.*, *Am. J. Manag. Care.*, 8(17Suppl):S502-517, 2002.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Therapeutic use of the compounds in treating any or all pain from various diseases and disorders that require inhibiting COX-2 activity.

2) The state of the prior art: Publications expressed that treating acute and chronic pain caused by diseases or disorders by the inhibition of COX-2 is still exploratory. See *Stichtenoth et al.*, and *Hochberg MC.*, cited above.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for treating any or all pain arising from any or all diseases or disorders of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of

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enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples to show treating any or all pain and the state of the art is that the effects of inhibiting COX-2 activity are unpredictable and at best limited to modulation of rheumatoid arthritis.

6) The breadth of the claims: The instant claims embrace any or all pain due to diseases and disorders related COX-2 activity.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of receptor-ligand interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating the variety of pain arising from diseases by the instant compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the

application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).” That conclusion is clearly justified here. Thus, undue experimentation will be required to make Applicants’ invention.

Allowable Subject Matter

Claims 1-9, 11, 14, 20, 27-31 and 36-40, barring finding of any prior art in a subsequent search, are allowed.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you

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have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).


Venkataraman Balasubramanian

5/21/2006